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Brief report

Household level SARS-CoV-2 sero-epidemiology in a high prevalence group of adults and children-implications for community infection control

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In 108 households (n = 474, 280 ≤ 18 years old), SARS-CoV-2 seroprevalence was significantly associated with age (range 37.5%-78.7%) and lowest in children ≤ 10 years old. Among 92 households with members ≤ 18, 14 (15.2%) had only a seropositive child or adolescent, while 16 (17.4%) had only seropositive adults. Households with both groups concurrently seropositive (n = 62) were larger in size (mean 8.11 ± 2.49) vs (mean 5.77 ± 2.31) ($P < .001$).

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INTRODUCTION

The sero-epidemiology of Coronavirus disease 2019 (COVID-19) at a household level has been assessed through screening contacts of medically attended adult index cases, using cohorts with limited numbers of infected children, and/or outside the United States.[1-3] We report severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seroprevalence in a random group of large households sampled in the community.

METHODS

This study was conducted in an orthodox Jewish village in New York State, led by the local community health center and approved by the Western Institutional Review Board. A random sample of households from the community directory were invited to participate. After informed consent and assent, a phone survey ascertained household composition, overall compliance with preventive measures, history of COVID-19 symptomatology and medically attended disease in household members. Households with currently symptomatic members were excluded. Serum samples for individuals in recruited households were collected at the local health center. SARS-CoV-2 serology was measured using a previously validated assay.[4,5] Chi-squared or Fischer's exact tests were used to compare proportions, and 1-way ANOVA with Tukey multiple comparisons tests used to compare continuous variables. Analyses were performed using R version 4.0.0 (R Foundation for Statistical Computing).

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Conflicts of Interest: The Icahn School of Medicine at Mount Sinai has filed patent applications relating to SARS-CoV-2 serological assays and NDV-based SARS-CoV-2 vaccines which list Florian Krammer as co-inventor. Mount Sinai has spun out a company, Kantaro, to market serological tests for SARS-CoV-2. Florian Krammer has consulted for Merck and Pfizer (before 2020), and is currently consulting for Pfizer, Seqirus and Avimex. The Krammer laboratory is also collaborating with Pfizer on animal models of SARS-CoV-2.

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Table 1
Population sampled, seroprevalence and quantitative measures (endpoint titer) of IgG and IgM across age groups

Age group (years)*	Population eligible	Population sampled n (% eligible)	IgG positive n,%† (95%CI)	IgM positive n,%† (95%CI)	Quantitative IgG Mean (SD)	Quantitative IgM Mean (SD)
>1-5	117	48(42.7%)	18,37.5% (25.2%-51.7%)	7,14.5% (6.9%-27.5%)	362 (607)	55.8 (49.3)
>5 to 10	139	105(76.9%)	55,52.3% (42.9%-61.7%)	44,41.9% (32.9-51.5%)	526 (857)	88.8 (122)
>10-18	190	127(67.9%)	100,78.7% (70.7%- 85.0%)	78,61.4% (52.7%-69.4%)	656 (658)	125 (143)
>18 to 60	225	174(80%)	134,77.0% (70.2%-82.7%)	111,63.8% (56.4%-70.6%)	537 (735)	137 (256)
> 60	26	20(80.8%)	15,75% (52.75%-89.2%)	11,55% (34.2%-74.2%)	1946 (5625)	174 (207)

*27 infants in eligible households were not sampled.
†Percentage of those sampled.

RESULTS

Interviews and sample collection were done from January 3, 2021 to January 21, 2021. Among 6,800 households in the directory, 300 were invited to participate and 108 were enrolled, consisting of 724 individuals. Median household size in the enrolled sample was 6.5 (IQR: 4-9). No households reported COVID-19 related hospitalizations or deaths. While all households reported members with COVID-19 symptoms in the past 3 months rarely was the first symptomatic person ≤ 18 years (9 households, 8.3%). Only 29 households (26.8%) had members who previously tested SARS-CoV-2 PCR positive. Of 724 enrolled participants, 474 (65.5%) had samples drawn (Table 1) including 280 (59.1%) children and adolescents. The rate of SARS-CoV-2 seroprevalence was higher for IgG (n = 322, 67.9%) than IgM (n = 251, 50.4%). Nearly all households (99, 91.6%) had an IgG seropositive member. There were no significant differences in household size, composition and reported compliance with infection prevention measures between seropositive and seronegative households. Rates of IgG and IgM seroprevalence significantly differed across age groups and were lowest in children ≤ 10 years (Table 1, $P < .001$).

Among 92 households with members ≤ 18, 14 (15.2%) had only a seropositive child or adolescent, while 16 (17.4%) had only seropositive adults. Households with at least 1 adult or child/adolescent concurrently seropositive (n = 62) were larger in size (mean 8.11 ± 2.49) vs (mean 5.77 ± 2.31) ($P < .001$), and had a higher mean proportion of members ≥10 years (61.6% ± 0.19 vs 51.8% ± 0.18, $P = .02$). Quantitative IgG levels were significantly higher in older adults (Fig 1) but IgM levels were similar across age groups.

DISCUSSION

In this analysis of one of the largest community-based samples of SARS-CoV-2 infected children in the US, few children were diagnosed previously, and symptomatic index cases were mostly adults. This confirms that the bulk of pediatric SARS-CoV-2 infections[6] are not medically attended, and that active case detection is required. Exposure risk to children in this close- knit community is high,[7] which could explain higher pediatric seroprevalence rates compared to previous data.[1] The significantly lower seroprevalence rate noted in ≤10 year-olds may reflect less susceptibility to household SARS-CoV-2

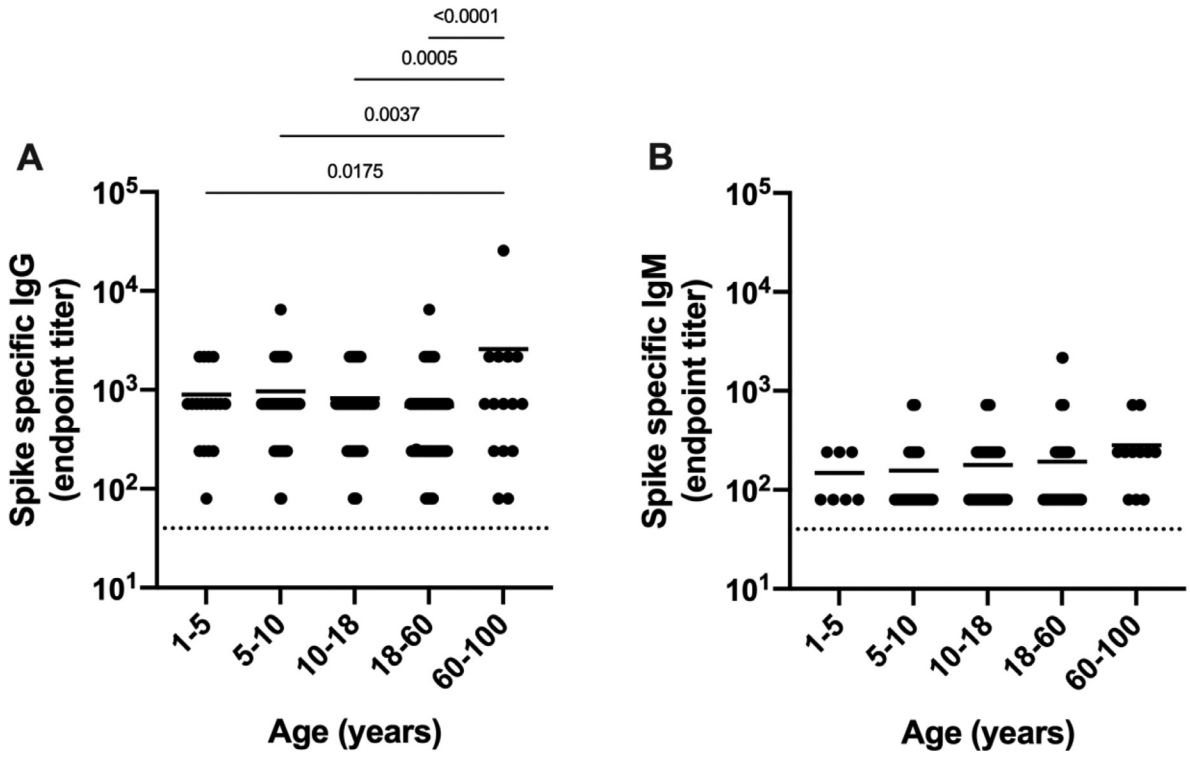

Fig 1. Antibody titers in seropositive individuals across age. Serum samples from household members that tested positive for antibodies against a recombinant version of the receptor binding domain (RBD) from SARS-CoV-2 spike were further tested in a semi-quantitative manner for IgG (A) and IgM (B) antibodies against the recombinant full-length spike. Stratification by age (X axis) of antibody endpoint titers (Y axis) is presented. Ordinary 1-way ANOVA with Tukey multiple comparisons tests is shown.

exposure, strengthening an emerging hypothesis from tracing and community-level serosurveys.[8] Similar but small proportions of households had adults and children with differing serostatus, indicating that either group could serve as index cases, a finding harder to replicate with contact tracing investigations considering higher rates of asymptomatic pediatric infection. Larger households were more likely to have concordant serostatus between adults and children, indicating household size as a risk for SARS-CoV-2 transmission between adults and children. Though epidemiologically plausible, this observation has not been demonstrated previously. Seroconcordant households also had a higher proportion of adolescents and adults, both potentially more vulnerable groups based on these data. Serum IgG levels were the highest in older adults, as observed previously,[9] but antibody levels were mostly comparable across age groups, a finding that gives context to potentially divergent antibody responses based on age in severe disease.[10] This study is limited by the lack of accurate timing of index infection but evidence of robust antibody responses in children even after mild or asymptomatic infection strengthens our conclusion of different seropositivity rates.[11] Another limitation is the difference in enrolled proportions between groups but this is less likely to cause a systematic bias that changes the conclusions.

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